UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/234,290	01/20/1999	LINDA C. BURKLY	10274/008003	6288

26161 7590 03/10/2004

FISH & RICHARDSON PC
225 FRANKLIN ST
BOSTON, MA 02110

EXAMINER	
UNGAR, SUSAN NMN	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 03/10/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/234,290	BURKLY, LINDA C.	
	Examiner	Art Unit	
	Susan Ungar	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE ____ MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *13 January 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *21 and 31-35* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *21 and 31-35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

1. The Amendment filed January 13, 2004 in response to the Office Action of July 15, 2003 is acknowledged and has been entered. Previously pending claims 26-30 and 38 have been canceled. Claims 25 and 31-35 are currently being examined.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

3. The following rejections are being maintained:

Claim Rejections - 35 USC § 112

4. Claims 25 and 31-35 remain rejected under 35 USC 112, first paragraph for the reasons previously set forth in the paper mailed July 15, 2003, Section 3, pages 2-5.

Applicant argues that (a) the fact that a soluble fibronectin polypeptide did not work as an inhibitor of VLA-4 in two specific non-diabetes related *in vitro* systems does not mean that the claims are not enabled, (b) at the time the application was filed, fibronectin polypeptides were known inhibitors of the VLA-4 activity, (c) once a correlation between inhibition of VLA-4 activity and the treatment of diabetes with anti-VLA-4 antibodies is demonstrated, similar results are expected using fibronectin polypeptides, (d) although Examiner has cited two references where an EILDV-containing fibronectin peptide fails to inhibit a VLA-4 activity, Examiner has ignored the numerous references showing that a CSA containing fibronectin peptide works to inhibit a VLA-4 mediated mechanism and cites Elices et al, Dinther-Janssen et al, Molossi et al and Korom et al, (e) the fact that EILDV containing peptides did not work in two specific references unrelated to diabetes does not mean that the claims are not enabled. The argument has been considered but has not been found persuasive because (a')(b')(c') it is clear from

the prior art references that VLA-4 has two known ligands (fibronectin and VCAM-1) which interact with VLA-4 at distinct binding sites. The prior art references clearly demonstrate that the action of anti-VLA-4 antibodies is **NOT** predictive of VLA-4 inhibitory activity of fibronectin peptides comprising EILDV. Although the demonstrations were done *in vitro*, given that fibronectin polypeptide comprising EILDV was in contact with cells which expressed VLA-4 for the entire exposure period, if it was the fibronectin binding site that was involved with inhibition of VLA-4 activity, then the activity would have been inhibited. If there had been inhibition, this might be suggestive that a similar inhibition might occur *in vivo*. However, given that there was no inhibition *in vitro* and that it was known in the art that *in vivo* exposure at the target site could well be delayed or inadequate due to variables such as biological stability, half-life, clearance from the blood, proteolytic degradation and immunological activation against the polypeptide, it would not be expected and no one of ordinary skill in the art would believe that it was more likely than not that the fibronectin polypeptide comprising EILDV would inhibit VLA-4 activity *in vivo* in those systems. Although it was known that fibronectin polypeptides were inhibitors of VLA-4 activity, it was also known that fibronectin polypeptides were not inhibitors of all types of VLA-4 activity as demonstrated by the prior art references. It is clear that it cannot be predicted, in the absence of objective evidence, that the claimed fibronectin polypeptide comprising EILDV will function as claimed. Although Applicant has established a nexus between anti-VLA-4 activity and the treatment of diabetes, for the reasons set forth previously and above, Applicant has not established a nexus between the claimed fibronectin polypeptide comprising EILDV and the treatment of diabetes, (d') Applicant cites four references which

were not found in the file. It is presumed, given that no reference was made to submission of the references, that the references were not in fact submitted, thus the information drawn to these references cannot be fully evaluated. However, it appears from Applicant's summaries that the references are drawn to demonstrations that either anti-VLA4 antibody or EILDV containing peptides inhibit VLA4 activity in rheumatoid arthritis patients (Elices et al), that EILDV containing peptides inhibit VLA4 activity better than anti-VLA4 antibodies in inflamed synovium (Dinther-Janssen et al), EILDV containing peptides inhibit VLA4 activity/binding to fibronectin (Molossi et al), and EILDV containing peptides inhibit VLA4 activity in chronic rejection (Korom et al). It is further noted that none of these references appear to be drawn to the treatment of diabetes. Given that VLA-4 is known to have two ligands, it is not surprising that EILDV containing peptides would inhibit VLA4 activity in some cases. However, given the prior art references, for the reasons set forth previously and above, in the absence of objective evidence, it cannot be predicted that the EILDV containing peptides would function as claimed in the treatment of insulin dependent diabetes, (e') the fact that Applicant cites four specific references unrelated to diabetes does not mean that the claims are enabled. Applicant's arguments have not been found persuasive and the rejection is maintained.

5. All other objections and rejections recited in paper mailed July 15, 2003 are withdrawn.

6. No claims allowed.

7. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. § 1.136(a).

A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF

THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. § 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan Ungar, PhD whose telephone number is (703) 305-2181. The examiner can normally be reached on Monday through Friday from 7:30am to 4pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvette Eyler, can be reached at 571-272-0871 The fax phone number for this Art Unit is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Effective, February 7, 1998, the Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1642.

Susan Ungar
Primary Patent Examiner
March 9, 2004